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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,341	11/20/2006	Guido Rasi	SCIC-050/01US 191485-2751	4578

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EXAMINER	
LIEB, JEANETTE	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/551,341	RASI ET AL.
	Examiner	Art Unit
	JEANETTE LIEB	1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)	
1) ☒ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.	6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :08/10/2010, 09/28/2009,04/06/2009, 08/11/2009, 03/13/2009, 06/06/2007, 06/06/2007.

Detailed Action

Applicants have submitted in their response filed on 03/15/10 that each of Chretien, Goldstein, Knutsen and Rudolph teach a method of preventing Aspergillus infection by administering thymosin alpha 1(TA1), because such a method is allegedly inherent in administering thymosin alpha 1 to patients, these references do not teach a method of treating Aspergillus with TA1, but a method of preventing Aspergillus. These rejections were withdrawn in the advisory action of 05/07/10. Applicants have also asserted that the combined teachings of Wingard and Knudson do not render obvious a method of treating a patient infected with Aspergillus. In light of the amendments, this 103(a) rejection has been withdrawn.

Applicants have amended the application to include a method of treating an infected patient in need thereof for Aspergillus with TA1 and Amphotericin B. In consideration of these amendments, an office action on the merits follows.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-8 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over in view of Knutson et. al. (WO 98/35696 A1) in view of Lass-Floral et. al. (*Pulmonary Aspergillus Colonization in Humans and its impact on management of critically Ill Patients*, BRITISH JOURNAL OF HEMATOLOGY, Vol. 104, p745-747, 1999), and as evidenced by Medline (Aspergillosis-

Symptoms and Treatment, http://www.nlm.nih.gov/medlineplus/ency/article/001326.htm, last visited June 15, 2011).

Knutsen et. al. teaches the administration of TA1 to mammals or patients in need of bone marrow transplants in order to promote T-cells (Th-1) that would have originally been derived from precursor cells in bone marrow (p. 1, lines 11-16). This reference also teaches that TA1 can be administered at various dosages such as 65 micrograms/body weight to .1-10mg (p. 19, lines 15-27). This reference further teaches that these patients (humans), and those which are HIV positive, are immune-compromised and in need of T-cell replacement (p. 19, lines 1-8). Additionally, administration to any patient necessarily 'prevents' Aspergillus infections, including invasive Aspergillosis.

Lass-Floral et. al. teach that fungal pathogens which cause pulmonary Aspergillus colonization are a common source of life-threatening infections to an immune-compromised host (See. P. 745, Abstract, See para. 1). This reference also teaches that the prevention of further aspergillus spore uptake is indispensible in preventing invasive pulmonary aspergillosis (p. 745 para. 1). This reference further teaches that if patients who are predisposed to aspergillosis are treated in laminar airflow units before starting severe immunosuppression, this may allow the host defiance to eliminate aspergillus spores present by preventing the accumulation of more spores (p. 746, Col. 2, para. 4).

As evidenced by Medline, People with allergic aspergillosis usually get better gradually, with treatment, but it is common for the disease to come back (relapse) and need repeat treatment. Further, Medline provides evidence that if invasive aspergillosis does not get better with drug treatment, it eventually leads to death, but what happens to a person with invasive

aspergillosis also depends on the underlying disease and immune system function (See http://www.nlm.nih.gov/medlineplus/ency/article/001326.htm) .

It would have been obvious to one of ordinary skill in the art at the time the invention was made to give an immuno-compromised patient infected with Aspergillus an effective dosage of TA1 as taught by Lasso-Floral et. al. One would have been motivated to treat an already infected patient with TA1 because one of the symptoms of aspergillus infections is further infection by additional colonies of spores that exacerbate the disease.

There is a reasonable expectation of success that TA1 administration will effectively treat patients infected with Aspergillosis by preventing the spread of spore colonies.

As to the dosages of TA1, it would have been obvious to optimize to dosages to obtain the most effective result.

The MPEP states:

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be *prima facie* obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler,* 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

Thus, the claims are rendered obvious over the prior art.

1. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over in view of Knutson et. al. (WO 98/35696 A1) in view of Lass-Floral et. al. as evidenced by Medline and in further view of Wingard et. al. (Bone Marrow Transplantation (1997) 19, pages 343-347).

The combined teachings of Knutson and Lass-Floral as evidenced by Medline are discussed supra.

The difference between the prior art and the instant claims is that those references do not teach the administration of amphotericin B.

Wingard provides that amphotericin B is well known for treating Aspergillus infections related to bone marrow transplants (See Abstract). This reference further teaches that Amphotericin B is the mainstay of antifungal treatments for serious fungal infections such as Aspergillus spores in patients with bone marrow transplants (p.343, Col. 2, para. 2-3).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used TA1 As taught by Knutson and lass-Floral in combination with the Amphotericin B as taught by Wingard because they both treat Aspergillus in humans in need of bone marrow transplants. One would have been motivated to add Amphotericin B to the composition TA1 because both treat different aspects of invasive Aspergillosis.

There is a reasonable expectation of success that a combination of A1 and Amphotericin B would treat Aspergillus as is known in the art.

As to the dosages Amphotericin B, it would have been obvious to optimize to dosages to obtain the most effective result as discussed supra.

Thus, the claims are rendered obvious over the prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JEANETTE LIEB whose telephone number is (571)270-3490. The examiner can normally be reached on 8:30am -5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JEANETTE LIEB/
Examiner, Art Unit 1654

/Cecilia J Tsang/
Supervisory Patent Examiner, Art Unit 1654